

REMARKS

Claims 6-12 and 14 are pending. Claims 6-8, 10, 12 and 13 are rejected under 35 U.S.C. § 103(a) over Litborn (WO9833052) in view of Hawkins et al. (US Pat No. 5,198,353). Claims 9 and 11 are rejected over the same plus Mian (US Pat No. 6,319,469).

The Examiner's rejections are founded on combining Litborn and Hawkins. Applicant respectfully disagrees with the Examiner on the content of the Hawkins disclosure, and the propriety of combining the two references.

Hawkins uses the known technique of acetone precipitation of proteins. Contrary to the Examiner's understanding, acetone is not an aqueous solution but is an organic solvent. *See* Hawkins, claim 10. Depending on the ionic strength of an aqueous solution, acetone may or may not be miscible with the solution.

An obviousness assessment has several criteria and imposes a significant burden of proof on the Examiner. MPEP § 2142. The possibility alone of the miscibility of acetone and water cannot sustain a rejection under 35 U.S.C. § 103(a).

For example, the initial issue in an obviousness inquiry is what is the scope of the relevant art. MPEP § 2141.01 Subsumed within and defining this inquiry is the issue of analogous art. MPEP § 2141.01(a). The Hawkins reference needs to be "in the field of applicant's endeavor" or the Hawkins disclosure needs to have content that "logically would have commended itself to an inventor's attention in considering his problem." *Id.* Hawkins is not in the field of fluid sample volume stability or microfluidic devices. Further, when considering the problem of fluid sample volume stability, there is nothing in Hawkins disclosure of protein precipitation procedures that would "commend itself" to someone trying to solve the problem of fluid sample volume stability addressed by the pending application. Hawkins is dealing with much larger volumes than the microvolumes the present invention is dealing with and the proportional volume of evaporated liquid is insignificant compared to the total volume and does not constitute a problem.

Next there are several legal prohibitions that preclude combining some references. One is the principle that the combination of references cannot make the resultant product or process incompatible with its intended use(s). MPEP § 2143.01 (V). The Hawkins and Litborn combination is a case on point. The purpose of the pending claims is to stabilize fluid volume in a microvolume sample to avoid concentration changes of reactants due to evaporation. If the reaction is a chemical one, replenishing with acetone and continuously increasing the acetone percentage in the solution would not be compatible in many if not most circumstances. This would be even more so for cell, affinity or enzymatic based assays because the acetone percentage would increase until it interfered with the normal functions of the cell or protein reactant and eventually would kill the cell or denature/precipitate the protein, meaning that such reactants are withdrawn from a desired reaction (decrease in concentration of active reactant). Thus, one of skill would not consider Hawkins useful for addressing the problem to be solved because the Hawkins method of protein precipitation is incompatible with the purpose of the methods claimed.

Finally, a core legal principle guiding obviousness judgments is the question of motivation to combine or modify a cited reference to yield an embodiment within the pending claims. MPEP § 2143.01 (I).

Procedurally, the analysis and validation of a motivation to combine must be specific, thorough and searching. *Id.*; *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002). The Examiner uses sparse and conclusory statements discussing the alleged motivations to combine:

the ability to extract components. One would use acetone as the covering liquid in order to precipitate out and collect (or analyze) the protein compounds without having to evaporate the sample or covering liquid. This would save processing time.

Examiner's Office Action Dated 02/08/06, pg 4, first full sentence. The rationale that "[t]his would save processing time" is indistinguishable to the ones the *In re Lee* court rejected. *Id.* at 1343 (Conclusory statement that 'another motivation would be that the automatic

demonstration mode is user friendly and it functions as a tutorial' did not adequately address the issue of motivation to combine.)

Substantively, the Examiner's motivation is misplaced. An acetone precipitation to recover proteinaceous products would occur after or be used to terminate a reaction. The pending claims are drawn to "replacing solvent continuously...wherein the microvolume of solvent comprises reactants for performing a reaction..." This relates back to the incompatibility of Hawkins and Litborn and the nonanalogous art discussions above. Applicant respectfully suggests these issues may not have been appreciated by the Examiner because of the misperception of acetone as a form of aqueous fluid rather than an organic solvent. Further, if the precipitate is to be collected/analysed as suggested in the quoted part of the Office Action, the acetone/water solvent has to be removed anyhow. Evaporation of microvolumes of acetone/water is rapid. Applicant cannot therefore understand the time-saving advantage suggested in the Office Action.

In view of the above, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02149US0 from which the undersigned is authorized to draw.

Dated: May 8, 2006

Respectfully submitted,

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